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The Treatment of Phthisis.

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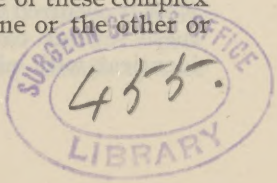
THE TREATMENT OF PHTHISIS.

Mr. President, Ladies and Gentlemen : I will not occupy your time very long as my colleague has gone pretty thoroughly into the explanation of our work in giving you our pathological ideas; I shall speak to you only from a clinical standpoint. It is the predominating opinion of physicians that the bacillus tuberculosis is the specific and only cause of the several forms of disease known as tuberculosis, and from its behavior it is a very hard thing to explain away. But when we consider from a clinical standpoint this bacterium, as the cause of the several conditions, known as tuberculosis, phthisis pulmonalis, in its several forms, tuberculous joint disease, scrofulosis, so-called tubercular skin diseases, bone disease, some forms of leprosy, besides other complex affections, it must strike any one who will think of it for a moment, as being impossible!

With regard to the bacillus, of course its specific character we do not question at all; nor its value as a diagnostic sign. The results observed are explained on the theory that it should have a nidus, and upon this nidus develop the disease, or, that it may remain latent in the body, constituting animal parasitism, a condition which was foreshadowed by Dr. Lionel Beal, twenty years ago, or that the bacillus is imbibed, exists for a time in a latent state and is then eaten up by leucocytes or by other microbes — phagocytosis. Now if the bacillus be *the* cause of these complex conditions we must recognize one or the other or all of these theories.



We have in phthisis pulmonalis, as you are well aware, three distinct clinical types of disease. It is almost impossible, so far as I know, to distinguish acute phthisis from miliary tuberculosis, the course is rapid in both, the temperature makes about the same range in each, about the same class of individuals are effected and present about the same symptomatology, which I will not detain you by describing. There is another form which we may properly denominate the *subacute form*, in which the patient has a distinct catarrhal inflammation, existing for a certain length of time, in the mucous membranes of the bronchial tubes, with little or no constitutional disturbance at first, but simply local disturbance, cough and respiratory sensations, while, sooner or later constitutional disturbances come on, and we find, if we make frequent observations by physical examination that the inflammation is extending to the smaller tubes, and involving the air cells ; finally, if the process goes on there is continued wasting, more pronounced constitutional disturbance, hyperpyrexia, etc., and breaking down of the tissue, involving bronchii and alveoli of the lung and resulting in that peculiar suppuration called caseation, if we examine such a patient at the end, upon the post-mortem table, we find cavities, caseous matter, indurated places and other evidences of inflammation. There is still another form, called *chronic*, in which there is the same result but the march is much slower, the constitutional disturbance also is put off for a long period, but after awhile, if the patient live long enough, the same condition of breaking down—caseation and induration occurs, and we have about the same morbid anatomy for chronic phthisis pulmonalis. Now it occurred to us in common with many that these several conditions could not possibly be identical with either that condition of bone or

peritoneal disease where no bacillus is found, or with general tuberculosis, a general or constitutional disease which exists from the beginning. It occurred to us also that phthisis pulmonalis could not be exactly the same clinically as the disease in the lower animals which is induced by inoculation, and therefore we began to look about for some other cause or causes. In other words, it seemed incomprehensible to me as a clinician, and to Dr. Gibbes as a pathologist, that this *one bacterium* could possibly be alone, the cause of these several complex diseases, because, as you know, reasoning from analogy that each of the specific fevers and like diseases show pretty constant phenomena, and so on, are alike or nearly so, and although there may be a seeming connection between some forms, perhaps, as between the typhoid condition and typhoid fever, yet the causes are not necessarily alike. We therefore, while not contending against the universal existence of the bacillus tuberculosis, think it probable that it is more of a concomitant or resultant in determining certain conditions. This thought, however, is not new; that something else beside the bacillus operates in this disease, for it was suggested by our worthy presiding officer, Dr. N. S. Davis, in 1882, in a paper before the American Medical Association, in which he said that there must be some chemical or biochemical action besides this bacterium to account for such conditions and courses; and many other clinicians have expressed the same doubt. But the thing is to work it out. One more word, concerning the infectious character of the disease; it is argued by clinicians in Europe and a great many in this country, that dry sputum when breathed by an animal or man will produce phthisis pulmonalis! this is true! for we have produced the disease in monkeys by insufflation of

sun-dried sputum. In this way we have produced true acute and subacute phthisis pulmonalis, the disease being located *in the lungs*, while by inoculation of monkeys the disease produced has been general, infecting the spleen, liver and other organs, and least or not much at all, the lungs.

It is stated by several bacteriologists and pathologists, even by Koch, I think, that if you dry sputum in *the sun* the virulence of the bacillus is destroyed. We have also found this to be true. Yet we have thus dried the sputum in the sun, and been able to produce the disease in monkeys by insufflation. Does not this seem to indicate that there must be *something* back of the bacterium which is an active agent? Will the absolutely dead and destroyed bacillus produce this effect? We were therefore by this led strongly to think that there is a bio-chemical action in this disease, determining the particular sort of degeneration and suppuration, known as caseation. This then is the main idea in our view and, moreover, we consequently believe that when the disease is in the lung tissue there the poison is generated, induced by long continued inflammatory changes having taken place. We also believe that ordinary subacute phthisis pulmonalis and some other forms are perhaps similar in their nature to what was called in the old fashioned parlance, scrofulosis. Now with such views we began using different things locally by inhalation to stop if possible the formation of the caseating process and source of chemical action.

It is unnecessary for me to tell you of the large number of experiments, mostly failures, which we have instituted; we used the several gases disseminated in different ways, hydrogen, oxygen, carbonic acid, hydrofluoric acid, etc., with sulphuretted hydrogen; through accident, we

discovered that it is a most virulent and subtle poison, one of our assistants in the laboratory was almost killed by it, besides a couple of monkeys killed outright. So we went on trying the gases, and finally settled upon chlorine, first used in 1828. From a study of its chemical nature as far as known, and from the fact that it is more or less combined with so many of the well known chemical reagents that are in use, it seemed to suggest itself to us as being very desirable for our purpose, but by causing so much irritation when inhaled, inducing so much inflammation by contact with animal tissues, it became a question whether we could introduce it or not; we tried a great many methods. First, mixed with air in small proportion and so on, and after killing a few monkeys and guinea pigs, we found after awhile that these animals could inhale the gas in the proportion of 1-40,000 of air ; but this dilution we discovered was not sufficient to destroy the virility of the sputum, so we increased the quantity of the mixture until obtaining one that would destroy the activity of sputum, so that an animal inoculated with it was not affected. We found that with a mixture of about 1-4000, (by exposure for a few moments) we would destroy the virulence of sputum, so that we could inoculate animals with such sputum without producing any disease. Observing, as we thought, that hydrochloric acid and hypochlorous acid was evolved very soon after the liberation of chlorine gas in the air, probably accounted for its irrespirability and was the cause of the irritation, because the monkeys died from common inflammation of the whole respiratory lining. This afforded very good study, however, because there was general broncho-pneumonia produced, therefore we felt as though we must go on very carefully and not induce such a condition in the human being.

After trying many different things to neutralize the by-products we succeeded in accomplishing the purpose by using a solution of chloride of sodium. We began with chlorine water spray, but found by experiments with guinea pigs in a gas cage that sprays did not penetrate into the lungs readily, that is without very long exposure although gas was evolved, all of which seemed to be unsatisfactory. It is possible, however, that the local effect of anything may be continued for a long time on the respiratory tract, beyond the place of contact, but we could get no chemical reactions in animals' lungs by using sprays, unless we used some substance subsequently giving off the gas. We obtained some effect from the spray of peroxide of hydrogen, which, after being diffused in the air of the gas cage, seemed to split up; also with chlorine water, which after awhile left the chlorine gas in the air, but we could not thus destroy the sputum. We therefore continued with our experiments in the use of chlorine gas, and found that with chloride of sodium spray well diffused, animals could inhale chlorine for a considerable length of time; and after trying it thoroughly on animals we began experiments on human beings with satisfactory results. Our idea was to *stop* the *formation* of the virus, whatever it might be, whether a ptomaine, a leucomaine or a toxalbumin, etc., and thus to stop the progress of the disease at these points, believing that phthisis pulmonalis is *essentially* a *local* disease. But we found after awhile that this plan would not *stop* the process altogether although it would check it! In the monkey, it would only feebly act in checking the course of the inoculated disease. But if we could manage to set up phthisis pulmonalis in monkeys by exposure, or from the insufflation of the dried sputum, or in menageries, we could prolong the course of the disease very much in-

deed by the gas. Constitutional disturbances would come on after awhile, however.

Turning attention toward meeting constitutional effects, the iodides of a great many chemicals were used, also chlorides and sulphides. We at first used them by the mouth, which brought serious events. On account of the changes which chemicals undergo in the stomach and intestinal canal we thought it better to use them by hypodermic injection if possible. There are reports in the literature of medicine from the last century, that iodine was valuable, but an irritant, and would produce abscesses, which it did in our experience. We thoroughly tried it, but had abscesses, which caused the death of the animals, but we found by accident that the abscesses were due to chemical impurities. After having the iodine resublimated by Dr. Clark we had no difficulty from abscesses, unless we used enormously large doses on animals. The same thing we found to be true of the chloride of gold and sodium and permanganate of potassium. The idea of using iodine came to us first from the fact of its resolvent action upon the lymphatic glands and tissues generally in all of those diseases which so closely resemble phthisis pulmonalis clinically. We have used also the arsenite of potassium, but found that the poisonous effect was so great that it could not be continued for any considerable length of time. We observed that after using iodine a certain length of time, a certain condition, iodism, took place which prohibited its further use; animals and man would have diarrhœa, vomiting, and would refuse food, etc. It is astonishing how much a little animal like a guinea pig can stand of these chemicals. These symptoms coming on soon made it necessary to have something else to hold the effect as it were. Taking our experience in the action of chloride of gold and so-

dium on dead tissues in general, we hit upon that, after failure with bichloride of mercury and other salts, and used it locally and by injection. Although it is said by surgeons that if you use hypodermic injections aseptically no abscess will follow, yet you will find that bichloride of mercury used hypodermically may produce abscess. This is not the case with chloride of gold and sodium if chemically pure, which, as you know, has been used for years as an alterative. We began by small doses and gradually increased them. We inoculated a number of guinea pigs, first with these chemicals, one series with iodine and one series with gold, and after doing that for a week or so until we noted physiological effects, we then inoculated them with well known virulent sputum and found to our astonishment that the pigs did not take the disease. We repeated this with another series, with the same effect, until we have now a number of very healthy pigs that have been inoculated with iodine and gold and with undoubted virulent sputum as proven by control animals. Just which is the better, of course has not been determined yet, for there are a great many things to learn. Unfortunately, the further we go into such a subject the more we appreciate that we know but little. We have been trying since, in continuance of our work, to trace out the poison, whatever it is. If we are right in this idea that it is a toxalbumin, a ptomaine, or a leucomaine, we want to isolate it. We want to get it out so that we can show it and test it and have it exposed in its true form, just as we can get crystals of strychnine, and we do not feel that the work is done unless the poison can be thus shown. We therefore feel that we are in the first part of the work only until we can show what part of these extracts lie at the bottom of the causation.

We are now engaged in making extracts — I can only hint at it, can only say that some of the results we have had from these extracts have been astonishing to ourselves, and if we can continue and perfect these investigations the probability is that in a year, or perhaps less, we may be able to isolate the particular poison or poisons which produce this disease, or which are generated in the body and keep up the disease. These extracts will produce it in the guinea pig; but whether they will do it *every time* we do not know; we have not had time to test it thoroughly.

I suppose some of you may want to know what success we have had with human beings. We have tried to be very careful about making promises, although we have been published in the papers very much more than we anticipated or desired and there have been a great many exaggerated statements made. But of course you would like to know what success we have had thus far. I cannot give you the details of the cases to-night, we expect to publish some case histories in a short time. Of the cases of so-called general tuberculosis we have treated altogether about four well-marked cases; two of which died without showing any effect of treatment, one of them is certainly very much better, and the other case is simply held in abeyance, so far as we can observe. We have treated a number of cases of phthisis pulmonalis, including what Dr. Gibbes spoke of as the tuberculous form and the pneumonic form. We have had in all about twenty-two cases under observation for about two to three months with about six so-called cures, taking all the several cases together, but there has not been time enough to tell whether these people have been thoroughly cured or not. In one case there was very decided laryngeal ulceration, which

was seen by several medical gentlemen, in that case the cicatrix was so complete that it could be seen with the laryngoscope, just before she went home about Christmas practically well; her physician continues the hypodermic injection about once a week. One case I have in mind was a man in whom the upper left lung was breaking down, as was evidenced by moist and gurgling râles, so that there could be no mistake about it. He was examined by two or three others besides myself. This man has been under treatment since September and he has now an injection about once a week or ten days, but has practically gone from under the treatment. Another case, that of a young girl, who has gone home, seems to be lasting, the last advice is that she has remained well with scarcely any cough, merely a little hacking in the morning. In her case the diagnosis had also been made out by physicians before she came to us. Another case is that of a teacher who has resumed her school duties since January, she still coughs a little in the morning but has no elevation of temperature now and is gaining flesh and strength. Another case was that of a man whose disease was of a more chronic form; he left the hospital in a very much better state; he eats well and has no elevation of temperature whatever, no nocturnal diaphoresis, or anything of that kind. Of course this does not prove anything until more time elapses.

We have now about thirty-five cases under treatment, some of which are doing very well! There are two or three of them termed "caseous pneumonia," that are not doing very well. The one case of tuberculosis which I mentioned is a case which several gentlemen outside the staff saw in the hospital; we thought of giving up the treatment, because there was no chance, for it is undoubtedly a case of general tuberculosis. But

after one or two relapses she has been getting better, and when I left home she had been sitting up considerably for a number of days past; although she has elevation of temperature she has no nocturnal diaphoresis, her appetite has returned and she expectorates only about two drams of mucous in twenty-four hours, with no pus. We have one case of a young boy in the hospital, which is very promising and very interesting inasmuch as the probability is that he had pneumonia followed by abscesses of the lungs first, and then caseation of the lung. Another case was of pneumonic abscess followed after a time by the presence of tubercle bacilli in the sputum; on account of the deep location of the abscess, I did not open into the lung. I was afraid to cut through such a large amount of lung tissue to reach it. I therefore put him under this treatment, and he is slowly recovering from the abscess of the lung.

There are some other chemicals we have been using lately that may prove more valuable than iodine and chloride of gold. Of course the experimentation is far from complete, but one of them especially bids fair to be more promising than gold. The general plan of treatment seems to us to hinge on the use of chlorine gas to stop the caseation as far as possible, and cut off the origin of the poison, which thence is circulating through the system. In the early stage of disease, before much caseation, we do not think it is necessary to use the chlorine gas too freely, but instead the iodine, for its well known effect upon chronic inflammation.

I would say in regard to the manipulation of chlorine gas that it is a very simple thing but it needs some care. The chloride of sodium spray should be put into the room first, and the air thoroughly laden with it before the chlorine gas

is evolved. At the hospital we use about 1-20,000 up to 1-4000. The first dose should be quite small for cases of laryngeal phthisis. In cases where there is ulceration chlorine gas in a room seems much the better way. If, however, there is only tumefaction the mixture of sol. of chloride of sodium and chlorine water chemically pure, is quite sufficient from an inhaler. The mixture of the two was suggested to us by Dr. Ingals, of your city. Before that, we used two tubes one containing chlorine water and the other the chloride of sodium solution. We had tried mixing them before but had always obtained a precipitate, and we therefore thought the two were incompatible, but we found out afterwards that it was because of exposure to light and long standing, and if the mixture be used immediately we could get good results. So in cases of laryngeal phthisis of all forms, we should recommend that an inhaler be used.

We are certainly very much obliged to the profession of Chicago for the attention that has been shown us. When we started out, we had no idea that we were going to interest the profession of Chicago to such an extent, and as I said, we are very grateful for the attention we have received, and feel that we do not deserve it. We have not accomplished anything as yet, we have only started! We have nothing definite to promise and we only hope that all of you may aid us in every way possible by your criticisms and by your crucial tests, for that is the only way in which this problem can be solved.